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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/900,294	07/06/2001	Carol T. Schembri	10990631-2	7409

7590 04/09/2004

AGILENT TECHNOLOGIES, INC.
Legal Department, DL429
Intellectual Property Administration
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EXAMINER	
SISSON, BRADLEY L	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 04/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/900,294	SCHEMBRI ET AL.	
	Examiner	Art Unit	
	Bradley L. Sisson	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 December 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *51-67 and 72-78* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *51-67 and 72-78* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *See Continuation Sheet*.

Continuation of Attachment(s) 6). Other: Notice to Comply with Sequence Rules.

DETAILED ACTION

Specification

1. The specification is objected to as documents have been improperly incorporated by reference. In particular, the specification states at page 15, line 8, and at page 21, lines 10-11, that "all patents, patent applications, and publications mentioned herein are hereby incorporated by reference." Such omnibus language fails to specify what specific information applicant seeks to incorporate by reference and similarly fails to teach with detailed particularity just where that specific information is to be found in each of the cited documents. As set forth in *Advanced Display Systems Inc. v. Kent State University* (Fed. Cir. 2000) 54 USPQ2d at 1679:

> Incorporation by reference provides a method for integrating material from various documents into a host document--a patent or printed publication in an anticipation determination--by citing such material in a manner that makes it clear that the material is effectively part of the host document as if it were explicitly contained therein. *See General Elec. Co. v. Brenner*, 407 F.2d 1258, 1261-62, 159 USQP 335, 337 (D.C. Cir. 1968); *In re Lund*, 376 F.2d 982, 989, 153 USPQ 625, 631 (CCPA 1967). **To incorporate material by reference, the host document must identify with detailed particularity what specific material it incorporates and clearly indicate where that material is found in the various documents.** *See In re Seversky*, 474 F.2d 671, 674, 177 USPQ 144, 146 (CCPA 1973) (providing that incorporation by reference requires a statement "clearly identifying the subject matter which is incorporated and where it is to be found"); *In re Saunders*, 444 F.2d 599, 602-02, 170 USPQ 213, 216-17 (CPA 1971) (reasoning that a rejection or anticipation is appropriate only if one reference "expressly incorporates a particular part" of another reference); *National Latex Prods. Co. v. Sun Rubber Co.*, 274 F.2d 224, 230, 123 USPQ 279, 283 (6th Cir. 1959) (requiring a specific reference to material in an earlier application in order to have that material considered a part of a later application); *cf. Lund*, 376 F.2d at 989, 13 USPQ at 631 (holding that **a one sentence reference to an abandoned application is not sufficient to incorporate from the abandoned application into a new application**). (Emphasis added.)

Accordingly, the cited documents are not considered to have been properly incorporated by reference and as such, have not been considered with any effect towards their fulfilling, either in

part or in whole, the enablement, written description, or best mode requirements of 35 USC 112, first paragraph.

Sequence Rules Compliance

2. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below or on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. See page 25 of the specification.

3. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 CFR 1.821(g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a). In no case may an applicant extend the period for reply beyond the SIX MONTH statutory period. Direct the reply to the undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the reply.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 51-67 and 72-78 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Attention is directed to the decision in *University of Rochester v. G.D. Searle & Co.* 68 USPQ2D 1424 (Fed. Cir. 2004) at 1428:

> To satisfy the written-description requirement, the specification must describe every element of the claimed invention in sufficient detail so that one of ordinary skill in the art would recognize that the inventor possessed the claimed invention at the time of filing. Vas-Cath, 935 F.3d at 1563; see also Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572 [41 USPQ2d 1961] (Fed. Cir. 1997) (patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention"); In re Gosteli, 872 F.2d 1008, 1012 [10 USPQ2d 1614] (Fed. Cir. 1989) ("the description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed"). Thus, an applicant complies with the written-description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572.

6. For convenience, claims 51 and 75, the only independent claims, are reproduced below.

51. (Currently Amended) A method for conducting a hybridization assay within an enclosed hybridization chamber, comprising:

(a) providing a device comprised of a (i) a substrate having a surface with at least a portion of said surface representing a hybridization region, wherein a plurality of oligonucleotide probes are bound to the substrate surface within the hybridization region and arranged in a spatially defined and physically addressable manner, and (ii) a cover which scalingly contacts the substrate surface about the hybridization region, wherein the cover and the hybridization region form an enclosure having an interior space comprising a hybridization chamber; and

(b) introducing into the hybridization chamber a sample fluid comprising (i) a target molecule which may hybridize to a surface-bound molecular probe within the hybridization region, (ii) a hybridization buffer, and (iii) a surfactant of a type and present at a concentration effective to substantially reduce nonspecific binding and promote mixing of components within the sample fluid; and

(c) mixing the sample fluid by moving a bubble within the hybridization chamber to displace the sample fluid and maintaining hybridization conditions within the hybridization chamber for a period of time sufficient to allow hybridization between the target molecule and a surface-bound molecular probe to occur;

~~wherein the surfactant is a polymeric nonionic surfactant which is polyethylene oxide.~~

75. (New) A method comprising:

(a) scalingly contacting a cover to a first substrate having a plurality of molecular probes bound to the surface of the first substrate to form a first sealed hybridization chamber about the substrate surface-bound molecular probes,

(b) performing a hybridization assay with the first sealed hybridization chamber and a sample comprising a target molecule which may hybridize to a surface-bound molecular probe,

(c) opening the hybridization chamber and removing the first substrate,

(d) reusing the cover by scalingly contacting the cover to a second substrate having a plurality of molecular probes bound to the surface of the second substrate, wherein the cover and substrate surface form a second sealed hybridization chamber about the substrate surface-bound molecular probes,

(e) performing a hybridization assay with the second sealed hybridization chamber and a sample comprising a target molecule which may hybridize to a surface-bound molecular probe.

7. The claimed method has been interpreted as encompassing the use of virtually any concentration of polymeric nonionic surfactant (polyethylene oxide) and where the hybridization chamber of the "device" has virtually and volume and is of virtually any dimension. A review of the disclosure, however, fails to find an adequate written description that would support such breadth of scope. In support of this position, attention is directed to page 15, which states:

> The surfactant generally represents between about 0.1 wt. % and 10 wt.% of the sample fluid, preferably between about 0.5 wt.% and 5 wt.% of the sample fluid, more preferably between about 0.75 wt.% and 5 wt.% of the sample fluid; however, it should be emphasized that the exact concentration will vary with the surfactant selected, and those skilled in the art may readily optimize the concentration with respect to the desired results, i.e., reduction of nonspecific binding and facilitation of mixing within the sample fluid. An exemplary sample fluid will contain between about 0.1 wt.% and about 1 wt.% of polyethylene oxide and between about 0.05 wt.% and about 1 wt.% lithium lauryl sulfate. (Emphasis added)

As can be seen above, at the broadest, applicant contemplated a range of from "about 0.1 wt. % and 10 wt.% of the sample fluid" where any nonionic surfactant was to be used, and then contemplated a range of from "0.1 wt.% and about 1 wt.%" when polyethylene oxide was being used. Such disclosure does not provide adequate support for a range that is without limits, as is the present case.

8. For purposes of examination, said claims have been interpreted as encompassing using a device of virtually any size, shape and dimension, that the surface-bound molecular probes can be directed to any nucleic acid of any coding or non-coding sequence as found in any and every life form, that the probes can be used in a simultaneous manner whereby multiplex assays where mixtures of related and divergent sequences are hybridized to the surface-bound probes and where no detectable label is used. Attention is also directed to page 13, last paragraph, bridging to page 14, of the specification, herein dimensions of the device are disclosed.

> This chamber height may range from about 0.002" to 0.02" (50 μm to 500 μm). The dimension of the cover, the peripheral lip, and the reaction area are such that the reaction area is generally in the range of about 4 mm^2 to 500 mm^2, preferably about 20 mm^2 to 350 mm^2, and the reaction chamber has a volume in the range of about 0.2 μl to about 312 μl, preferably about 1 μl to 200 μl.

As seen above, the specification does not provide an adequate description of the device to be sued in the claimed method whereby said device has virtually any surface area or chamber

volume. While applicant may argue that alternative device dimensions and alternative concentrations of surfactant would have been obvious to those of skill in the art, obviousness cannot be relied upon in satisfaction of the written description requirement. In support of this position, attention is directed to the decision in *University of California v. Eli Lilly and Co.* (Fed. Cir. 1997) 43 USPQ2d at 1405, citing *Lockwood v. American Airlines Inc.* (Fed. Cir. 1997) 41 USPQ2d at 1966:

> Recently, we held that a description which renders obvious a claimed invention is not sufficient to satisfy the written description requirement of that invention.

9. Accordingly, and in the absence of convincing evidence to the contrary, the claims are not adequately supported by the original disclosure such that the disclosure reasonably suggests that applicant was in possession of he claimed invention at the time of filing. Applicant is urged to consider narrowing the scope of the claims to those embodiments adequately described in the original disclosure.

Response to argument

10. At page 11 of the response received 08 December applicant asserts that the original claims provide support for the now claimed invention, directing attention to *Regents of the University of California v. Eli Lilly*. At page 12 argument is advanced that the examples cited in the prior Office action do not set the limits of the claimed invention, and quotes the specification where it is stated "those skilled in the art may readily optimize concentration with respect to the desired results." Applicant further directs attention to statements that the exemplary teachings, be they reaction volumes, device dimensions, etc., should not be construed as limiting the invention.

11. The above argument has been fully considered and has not been found persuasive towards the withdrawal of the rejection of claims under 35 USC 112, first paragraph. While agreement is reached in that literal support or the claim language may be present, the aspect of finding basis for claim language does not automatically translate in an adequate written description of same. As noted above, the specification must describe every element of the claimed invention in sufficient detail so that one of ordinary skill in the art would recognize that the inventor possessed the claimed invention at the time of filing.

12. For purposes of examination, the claims have been interpreted as broadly as is reasonably possible. The specification is reviewed to determine if every element of the claimed invention is also described in sufficient detail so that one of ordinary skill in the art would recognize that the inventor possessed the claimed invention at the time of filing. Applicant has not pointed to where the specification describes every element of the claimed invention so as to reasonably suggest that applicant was in possession of same. As noted above, the claimed method fairly encompasses the use of a device without limit, that the reaction can be performed with an infinite number of reactions simultaneously, and that probes are to be used which fairly encompass every nucleic acid sequence of interest, now and in the future. Applicant's arguments, however, fail to present convincing evidence as to where each and every element of the claimed invention is described so to reasonably suggest that the full genus of the claimed invention was in applicant's possession at the time of filing. Therefore, and in the absence of convincing evidence to the contrary, the rejection is maintained.

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

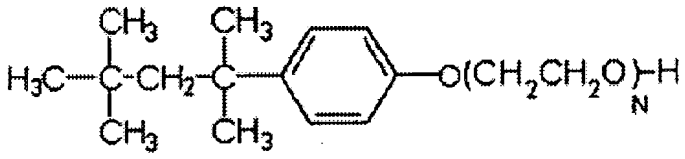
1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

15. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

16. Claims 51-67 and 72-78 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,229,297 (Schnipelsky et al.), or US Patent 5,154,888 (Zander et al.) in view of US Patent 5,856,174 (Lipshutz et al.), US Patent 6,184,029 B1 (Wilding et al.), and US Patent 6,030,787 (Livak et al.).

17. For purposes of examination, the term "polyethylene oxide" has been interpreted as encompassing any of the TRITON X surfactants. Support for this interpretation is based upon pages 13-14 of the disclosure, reproduced below.

> preferred. A preferred polymeric nonionic surfactant is polyethylene oxide, with particularly preferred polyethylene oxides comprising an alkylphenol ethylene oxide condensate. Such surfactants may be obtained commercially under the trade name "Triton" from the Sigma Chemical Company (St. Louis, MO), and including, for example, Triton X-100 (octylphenol ethylene oxide condensate) and Triton X-102 (also an octylphenol ethylene oxide condensate). More specifically, Triton X surfactants have been described as having the formula:



(I)

> in which N for Triton X-100 has an average of about 9.5 units per molecule while for Triton X-102 N is an average of about 12.5 units per molecule. Further information on both Triton X-100 and Triton X-102 can be found at the following Internet addresses: "www.sigma-aldrich.com/sigma/proddata/t6878.htm" and "www.sigma-aldrich.com/sigma/proddata/t6878x.htm".

18. Schnipelsky et al., disclose a device for use in conducting a nucleic acid amplification reaction and hybridizing the amplicons to immobilized probes. As seen in Figure 1, element **40** is directed to a hybridization chamber where probes are immobilized.

19. Schnipelsky et al., do not specifically disclose the volumes of the hybridization reaction or the use of a surfactant.

20. Zander et al., also disclose a device for conducting amplification reactions as well as hybridization reactions where a probe is bound to the surface of the device and is located within a hybridization chamber.

21. Like Schnipelsky et al., Zander et al., does not define the reaction volumes or the use of a surfactant, nor does either teach mixing the hybridization buffer in the chamber through use of a bubble.

22. Lipshutz et al., column 25, penultimate paragraph, teach "in come cases constant mixing within a single reaction/analytical chamber is desired, noting specifically PCR amplification reactions and hybridization reactions. The use of a hybridization chamber that comprises an array of oligonucleotides is specifically identified. Column 26, second paragraph, teaches using a mechanical and acoustic mixing means. Column 31, penultimate paragraph, teaches that acoustic mixing yielded the same results as mechanical mixing, which comprised the use of an incorporated bubble. In view of such teachings, the ordinary skilled artisan would have been moti9vated to have employed mechanical mixing means which incorporate at least one bubble for mixing fluids in a sealed chamber.

23. Wilding et al., disclose a device that is characterized as being "mesoscale." Dimensions of the fluid communicating means and chambers are found at columns 7-8. Such disclosures are considered to render obvious the presently claimed reaction volumes. Column 13 teaches specifically of having capture reagents bound to the support and that they may be located within a chamber.

24. The use of a surfactant in the hybridization reaction is not specifically disclosed.

25. Livak et al., column 16, penultimate paragraph, disclose using a hybridization buffer that comprises "Triton X-100."

26. It would have been obvious to one of ordinary skill in the art at the time that the invention was made to have modified the devices and associated method of either Schnipelsky et al., or Zander et al., with that of Lipshutz et al., Wilding et al., and Livak et al., whereby one of ordinary skill in the art would be able to effect hybridization reactions within a hybridization chamber that allows for mixing of hybridization buffer and wherein the hybridization buffer comprises a polyethylene oxide surfactant (Triton X-100). In view of the well-developed state of the prior art, and the detailed guidance provided, the ordinary artisan would have been both motivated and would have had a most reasonably expectation of success.

27. For the above reasons, and in the absence of convincing evidence to the contrary, the invention of claims 51-67 and 72-78 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,229,297 (Schnipelsky et al.), or US Patent 5,154,888 (Zander et al.) in view of US Patent 5,856,174 (Lipshutz et al.), US Patent 6,184,029 B1 (Wilding et al.), and US Patent 6,030,787 (Livak et al.).

Response to arguments

28. At pages 15-16 of the response of 08 December 2003 applicant notes that the references "do not each or suggest a step of mixing a sample fluid in a hybridization chamber."

29. The above argument ahs been fully considered and has been found persuasive. Accordingly, a new ground of rejection has been made against the amended claims. As noted above, the patent to Lipshutz et al., teaches using a bubble for mixing a sample fluid in a hybridization chamber

Conclusion

30. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

a. US Patent 6,420,114 B1 (Bedilion et al.)

b. US Patent 6,613,529 B2 (Bedilion et al.)

31. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

32. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

33. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (571) 272-0751. The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

34. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

35. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Bradley L. Sisson
Primary Examiner
Art Unit 1634

BLS
07 April 2004

Notice to Comply	Application No.	Applicant(s)	
	09/900,294	SCHEMBRI ET AL.	
	Examiner	Art Unit	
	Bradley L. Sisson	1634	

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☒ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☒ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☐ 7. Other:

Applicant Must Provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
For CRF Submission Help, call (703) 308-4212
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Technical Assistance.....703-287-0200
To Purchase PatentIn Software.....703-306-2600

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